Acta Dermatovenerol Croat 2016;24(4):261-267 CLINICAL ARTICLE

Assessment of Cardiovascular Risk Factors in Patients with Psoriasis

Olivia Komorowska[1], Michal Bohdan[2], Aneta Szczerkowska-Dobosz[1], Dorota Rawicz-Zegrzda[3], Maria Dudziak[3], Tomasz Zdrojewski[4], Marcin Gruchala[2], Dorota Purzycka-Bohdan[1], Roman Nowicki[1]

[1]Department of Dermatology, Venereology and Allergology, Medical University of Gdansk, Poland, [2]First Department of Cardiology, Medical University of Gdansk, Poland, [3]Department of Cardiac Diagnostics, Medical University of Gdansk, Poland, [4]Department of Preventive Medicine and Education, Medical University of Gdansk, Poland

Corresponding author:
Szczerkowska-Dobosz Aneta, MD, PhD
7th Debinki St.
80-211 Gdansk
Poland
adobosz@gumed.edu.pl

Received: January 17, 2016
Accepted: October 5, 2016

ABSTRACT Psoriasis is a chronic inflammatory skin disorder associated with increased cardiovascular risk. Aim of this work was to evaluate the association between psoriasis and chosen cardiovascular risk factors, echocardiographic parameters, and carotid intima-media thickness.

A total of 50 patients with psoriasis and 50 controls were enrolled in the study. Psoriasis area severity index was calculated in the study group. Systolic and diastolic blood pressure, body mass index, waist circumference, lipids, fasting glucose, and D-dimer levels were assessed in all patients. In addition, echochardiographic parameters and carotid intima-media thickness were measured.

Patients with psoriasis had higher blood pressure (P=0.001), elevated triglycerides (P=0.0218), lower high-density lipoprotein cholesterol (HDL-C) (P=0.0014), elevated D-dimer levels (p=0.0009), and were more frequently overweight (P=0.0198) in comparison to controls. There were no differences in echocardiographic parameters and carotid intima-media thickness between the psoriasis and control groups. Moreover, a positive correlation between psoriasis area severity index and blood pressure was observed (P=0.0088).

The study confirmed that psoriasis is associated with increased cardiovascular risk. The association between psoriasis, intima-media thickness, and echocardiographic parameters should be evaluated in large prospective studies.

KEY WORDS: psoriasis, cardiovascular risk, carotid intima-media thickness

INTRODUCTION

Psoriasis is one of the most common chronic skin disorders. It affects around 2.2-4.6% of the United States (US) population and is even more frequent in Scandinavian countries (1,2). Unfortunately, there are no available data concerning the prevalence of psoriasis in Poland, but it is estimated that it may affect approximately 2% of the population.

Despite intensive scientific efforts, the pathogenesis of psoriasis has not been fully understood. It has been postulated that psoriatic lesions may be the effect of complex genetic, immunological, and environmental interactions. Many clinical trials have proven that psoriasis may be classified as a chronic inflammatory systemic disease. It has been shown that the

inflammatory process in psoriasis is not limited only to the skin but may also significantly affect other organs, including the cardiovascular system (3,4). Chronic inflammatory process in this disorder may have a significant impact on the heart and blood vessels, affecting cardiovascular risk. It has been found that psoriasis may be associated with hypertension (5), obesity (6), dyslipidemia (7,8), diabetes, (9) and depression (10). In addition, some studies have reported increased carotid intima-media thickness (IMT) in patients with psoriasis in comparison with healthy controls (11). To our knowledge, few studies on IMT in psoriasis have been conducted so far in a Polish population.

Aims

The aim of the study was to assess the prevalence of chosen cardiovascular risk factors and biochemical parameters together with echocardiography and carotid IMT measurements in patients with psoriasis.

PATIENTS AND METHODS

A total of 50 Caucasian patients with plaque psoriasis and 50 controls matched for age, sex, and socioeconomic status were recruited from the region of Northern Poland for a single-center study. Participants of the study group were selected from the population of patients treated or consulted at the Dermatology Department over a period of 24 months.

There were 23 women and 27 men in the psoriasis group aged, 28 to 56 years (mean age ± Standard Deviation (SD): 42.4±7.8 years). Mean severity of psoriasis assessed using the Psoriasis Area Severity Index (PASI) was 22.4±9.2 (range: 12.4-45). Psoriasis duration time was 2 to 48 years (mean: 20.4 years). The beginning of the disease was calculated with regard to time in which onset of typical psoriatic skin lesions confirmed by a dermatologist occurred. The inclusion criteria were: severe plaque psoriasis diagnosed at least one year prior to recruitment, PASI of more than 10, the percentage of Body Surface Area (BSA) affected by psoriasis of more than 10, no psoralen combined with ultraviolet A (PUVA), methotrexate, cyclosporine, acitretin, or other anti-inflammatory agents at least 6 months prior to recruitment. The exclusion criteria were: pustular, guttate, or erythrodermic psoriasis, psoriatic arthritis (PsA) confirmed by a rheumatologist – patients with significant joint symptoms or other symptoms which may indicate PsA (i.e. dactylitis or enthesitis) were also excluded, as well as patients with a history of biologic treatment, patients with concomitant inflammatory skin disorders other than psoriasis, significant cardiovascular disease (confirmed coronary artery disease, heart failure, and valvular heart disease), confirmed diabetes, hypertension, dyslipidemia, or other chronic systemic diseases, and active cigarette smoking or history of smoking less than 5 years prior to recruitment. The control group consisted of 50 individuals (25 men and 25 women aged 30 to 50 years; mean age: 40.5±7.4 years) with no skin disorders, who were recruited from the study members' neighborhood or workplace due to similar socio-economic status (education, income, lifestyle) and were not related to the patients with psoriasis. Individuals with diabetes, hypertension, lipid disorders, chronic inflammatory diseases, and active cigarette smokers were excluded from the control group. In order to confirm control group was representative of the Polish population in terms of anthropometric measurements, blood pressure, and chosen biochemical markers associated with cardiovascular risk factors, it was compared with the NATPOL (12) study population of 1113 patients (523 women and 590 men, aged 30-55 years, mean age: 42.1±7.7 years). Physical examination with weight measurement, blood pressure, body mass index (BMI), and waist circumference measurements, blood samples including serum lipid levels, fasting glucose, and D-dimer level were assessed and compared in both analyzed groups. Dermatological examination with PASI score and BSA was performed in patients with psoriasis, while a total body skin exam was performed in the control group.

In addition, echocardiography, including left ventricular end-diastolic diameter (LVEDD), left ventricular end-systolic diameter (LVESD), intraventricular septum diastolic diameter (IVSd), posterior wall diastolic diameter (PWd), and left ventricular mass (LVM), was performed. Moreover, IMT of both common carotid arteries was measured using a 7.5/5.5 MHz linear array transducer in both groups. IMT measurements were obtained with the patient lying in the supine position and with the neck rotated to the opposite side of the examination. IMT was assessed using three different angle views for each carotid artery: transversal, longitudinal posterolateral, and anterolateral. We performed three IMT measurements for each near and far wall. A carotid IMT≥0.9 mm was considered subclinical atherosclerosis. All patients gave informed written consent before entering the examination. The study was approved by the Local Bioethics Committee (NKEBN/358/2010).

Statistical analysis was performed using STATISTICA 10.0 software. Quantitative variables were presented as mean or median value, Standard Deviation (SD), and 95% confidence interval (CI), while qualitative variables were presented as numbers and percentages. The Fisher exact test, Student t-test, χ^2 test,

Mann-Whitney test, and Kruskal-Wallis test were used for comparisons of categorical and continuous variables. For sample sizes less than 5, Yate's correction for continuity was used. The significance level for all tests was considered to be $P \leq 0.05$.

RESULTS

Overall characteristics of the study groups are presented in Table 1. Mean BMI was insignificantly higher in patients with psoriasis in comparison to controls and the NATPOL study group. There were no differences in BMI between the control group and the NATPOL study. The majority of the patients with psoriasis (70%, n=35) had a high BMI score with 32% (n=16) cases of overweight patients and 8 (n=16%) cases of obesity. In addition, mean waist circumference was significantly lower in the control group when compared to the psoriasis group and NATPOL study (Table 1). Mean systolic blood pressure (SBP) was significantly higher in the psoriasis group when compared to controls and the NATPOL study population (Table 1). In addition, diastolic blood pressure (DBP) was also significantly higher in patients with psoriasis in comparison with controls and the NATPOL population. DBP was also significantly higher in the NATPOL population in comparison with the control group (Table 1). Hypertension was observed significantly more often in patients with psoriasis in comparison with the control group and the NATPOL population. There were no statistically significant differences in the prevalence of hypertension between controls and the NATPOL study group. Hypertension was diagnosed in 66% patients with psoriasis (n=33), in 20% of controls (n=10), and in 32.3% of the patients in the NATPOL study (n=358). There were no significant differences in total cholesterol and low-density lipoprotein (LDL) cholesterol level between the analyzed groups (Table 1). Mean triglycerides levels were significantly higher in patients with psoriasis in comparison with controls and the NATPOL population. Moreover, HDL cholesterol levels were also lower in patients in comparison to the control group and the NATPOL population (Table 1). There were no differences in the fasting glucose levels between patients with psoriasis and the control group (Table 1). D-dimer levels were significantly higher in the population of patients with the analyzed dermatosis (Table 1). There were no significant differences in echocardiographic findings between the psoriasis and control groups. In addition, we did not observe any differences in IMT between the analyzed groups (Table 2). Moreover, a positive correlation between

Table 1. Characteristics of the analyzed groups

	Psoriasis (n = 50)	Controls (n = 50)	NATPOL study (n = 1113)	*P* value
Age (years)	42.4±7.8	40.5±7.4	42.1±7.7	NS
Men (n, %)	27 (54)	25 (50)	590 (53)	NS
BMI (kg/m^2)	29.6±7.1	26.2±4.1	26.5±4.7	NS
Waist circumference (cm)	101.8±16.4[1]	84.8±10.8[1,2]	101.8±16.4[2]	[1]*P*=0.0198 [2]NS
SBP (mmHg)	139.9±17.5[1]	124.1±12.5[1,2]	129.4±17.8[2]	[1]*P*=0.0001 [2]NS
DBP (mmHg)	88.8±11.1[1]	78.4±8.3[1,2]	82.6±10.9[2]	[1]*P*=0.0001 [2]*P*=0.0183
Glucose (mg/dl)	96.0±17.1	91.7±8.9	93.5±24	NS
TC (mg/dl)	211.9±51.3	203.8±36.2	204.7±39.5	NS
TG (mg/dl)	180.0±187.0[1]	119.6±57.9[1,2]	130.3±101.3[2]	*P*=0.0272 [1]0.0218 [2]>0.05
LDL-C (mg/dl)	131.8±40.6	124.9±34.4	129.3±32.0	NS
HDL-C (mg/dl)	45.5±12.5[1]	54.9±15.8[1,2]	50.2±14.0[2]	*P*=0.0022 [1]0.0014 [2]>0.05
D-Dimer	22.9±10.1	22±8.7	-	*P*=0.0009

Data are presented as mean ± Standard Deviation.

BMI: body mass index; DBP: diastolic blood pressure; HDL-C: high density lipoprotein cholesterol; LDL-C: low density lipoprotein cholesterol; PASI: psoriasis area severity index; SBP: systolic blood pressure; SD: standard deviation; TC: total cholesterol; TG: triglycerides; NS: not significant

Table 2. Echocardiographic parameters and carotid intima-media thickness measurements in the analyzed groups

	Psoriasis	Controls	*P* value
LVM (g)	216.01±87.23	188.62±58.40	*P*=0.2440
LVMI (g/m^2)	108.35±39.78	97.51±27.20	*P*=0.2806
RWT	0.38±0.07	0.38±0.08	*P*=0.9402
RWTc	0.41±0.07	0.39±0.07	*P*=0.2994
LVEDD (mm)	49.2±5.5	48.3±4.4	*P*=0.6075
LVESD (mm)	28.8±5.7	29.1±4.2	*P*=0.4928
IVS (mm)	10.8±2.3	9.9±1.9	*P*=0.0589
PW (mm)	9.3±1.8	9.0±1.8	*P*=0.5106
LVEF (%)	63.7±6.1	65.7±5.5	*P*=0.0767
IMT-R (mm)	0.58±0.10	0.56±0.11	*P*=0.3447
IMT-L (mm)	0.58±0.11	0.57±0.08	*P*=0.6673

Data are presented as mean ± Standard Deviation.

IMT-L: intima-media thickness-left side; IMT-R: intima-media thickness-right side; IVS: intraventricular septum; LVEDD: left ventricular end diastolic diameter; LVEF: left ventricular ejection fraction; LVESD: left ventricular end systolic diameter; LVM: left ventricular mass; LVMI: left ventricular mass index; PW: posterior wall; RWT: relative wall thickness; RWTc: relative wall thickness after correction

systolic and diastolic blood pressure and psoriasis severity measured using PASI score was found (SBP: r=0.65, *P*=0.0001; DBP: r=0.42, *P*=0.0027).

DISCUSSION

The results of many recent clinical and epidemiological trials confirm that psoriasis is not only limited to the skin but may also affect other tissues and organs, including the cardiovascular system. Several studies have shown that the incidence of cardiovascular risk factors is more frequent in patients with psoriasis (13,14). Fleming *et al.* (15) and Szponar-Bojda *et al.* (16) have reported that abnormal BMI values were significantly more often observed in this disorder. In our study, obersity evaluated by using BMI was also insignificantly more common in patients with psoriasis in comparison with controls. It is still not clear whether increased weight is a psoriasis risk factor or whether it appears as a consequence of the disease.

Szponar-Bojda *et al.* studied a Polish population of patients with psoriasis, showing that hypertension is more frequent in psoriasis (16). In this study, 40.17% of subjects with this disease had elevated blood pressure. Both systolic and diastolic blood pressure were significantly higher in comparison to controls (*P*=0.0004, *Z*=3.47 and *P*=0.036, *Z*=2.09, respectively). We also observed elevated blood pressure in the studied population. Both systolic and diastolic blood pressure were elevated significantly more often in comparison to the control group (66% vs. 30%). The correlation between hypertension and psoriasis is not well documented. It is believed that the chronic inflammatory process might be responsible for elevated blood pressure. Huskic *et al.* found that patients with psoriasis had a higher concentration of tissue angiotensin-converting enzyme in comparison to healthy controls (4.14U±0.34 vs. 1.86U±0.16, respectively) (17).

Lipid elevation is a well-known cardiovascular risk factor. There are hardly any data concerning hyperlipidemia in psoriasis in the Polish literature. Consistent with another study (18), we found significantly elevated triglycerides and lower HDL cholesterol levels in the analyzed group. Interestingly, in another study on a Polish population no differences in lipids except for increased HDL in patients with psoriasis were observed (19). The association between psoriasis and hyperlipidemia is not fully understood. It is possible

that the elevated cholesterol level may be a result of chronic inflammation with the decreased antioxidant activity that typically occurs in this dermatosis. On the other hand, cyclosporine and acitretin used in the psoriasis treatment may also lead to hyperlipidemia.

We found no significant differences in the fasting glucose level between analyzed groups. The results of the studies on glucose metabolism abnormalities in patients with psoriasis are conflicting. This may be explained by implementation of different diagnostic tools in various studies. Some scientists used the homeostasis model assessment of insulin resistance (HOMA-IR). Janusz *et al.* (20) analyzed a group of 42 patients with psoriasis with a negative history of cardiovascular diseases. Interestingly, they observed both increased insulin levels and HOMA-IR in patients with psoriasis in comparison with controls. The prevalence of increased fasting glucose in patients with psoriasis may be also associated with other common comorbidities found in this dermatosis: increased body weight and hyperlipidemia.

We also observed significantly elevated D-dimer levels in the study group. D-dimer is a novel cardiovascular risk factor and as such has been only analyzed in a few studies concerning psoriasis. Arias-Santiago *et al.* (11) have reported significantly increased level of acute phase parameters including D-dimer in 72 patients with psoriasis in comparison to 61 controls. This study has demonstrated that increased levels of fibrinogen and other acute phase parameters such as D-dimer may be associated with development of carotid atheroma plaques in psoriasis.

There are insufficient and conflicting data concerning echocardiographic parameters in psoriasis. Atas *et al.* (21) reported no significant differences between patients with psoriasis and controls regarding echocardiographic assessment of the left ventricle. Similarly to our results, the left ventricular mass index (LVMI) was insignificantly higher in the psoriasis group in comparison with controls (90.2±12.7 g/m^2 vs. 86.1±15.2 g/m^2; respectively). In another study (22), however, the authors observed a significantly higher incidence of left ventricular hypertrophy, wall motion abnormalities, and diastolic dysfunction in patients with psoriasis. In addition, Shang *et al.* (23) reported significant abnormalities in echocardiographic parameters in patients with psoriatic arthropathy. It is believed that the observed changes in this group may be the result of a more intensive inflammatory process and higher cardiovascular risk which is associated with it.

Increased carotid IMT is currently recognized as a cardiovascular risk factor. We found no significant differences between carotid IMT in patients with psoriasis and healthy controls. IMT, however, was found to be increased in various studies concerning psoriasis. Shahidi-Dadras *et al.* (24) have recently reported significantly higher carotid IMT in comparison to healthy controls (45% vs. 6.7%, P<0.0001). In addition, Robati *et al.* (25) observed that IMT in 60 patients with psoriasis was significantly higher than in the control group (0.65 mm vs. 0.43 mm, respectively, P<0.0001). On the other hand, a Dutch study (26) revealed no differences in IMT between 262 patients with psoriasis and controls. Lack of observed significant changes in carotid IMT in our study may be explained by the fact that the mean age in the study population was 42.4±7.8 years. Enrollment of older patients would likely have an impact on the statistical significance of IMT.

Furthermore, we found a positive correlation between psoriasis severity assessed by PASI score and blood pressure. On the other hand, we did not observe any correlation between PASI and obesity, lipid disorders, or diabetes, even though there have been such reports in large studies (5). Similarly to Balci *et al.* (27) we found no correlation between PASI and IMT. The majority of studies, however, revealed a positive correlation between PASI score and IMT (28,29).

Our study had several limitations. We did not have enough data concerning methotrexate therapy in the analyzed population of patients with psoriasis. This medication is currently widely used in the treatment of psoriasis in Poland. It has been shown that chronic treatment with methotrexate may reduce cardiovascular risk (30). Additionally, the study group was relatively small, but so far there have been no large multicenter studies on this issue in Poland. There is also no Polish registry covering patients with all types of psoriasis. Furthermore, it seems that the inclusion of other cardiovascular risk factors, such as high sensitivity C-reactive protein, in future studies may improve our knowledge of the Polish population of patients with psoriasis.

CONCLUSION

In conclusion, our study confirmed that patients with severe psoriasis have higher risk of arterial hypertension and increased waist circumference in comparison to the healthy population. Only blood pressure correlated with PASI. The association between psoriasis, IMT, and echocardiographic parameters should be evaluated in large prospective studies.

References:

1. Naldi L. Epidemiology of psoriasis. Curr Drug Targets Inflamm Allergy 2004;3:121-8.
2. Raychaudhuri SP, Farber EM. The prevalence of psoriasis in the world. J Eur Acad Dermatol Venereol 2001;15:16-17.
3. Reich K. The concept of psoriasis as a systemic inflammation: implications for disease management. J Eur Acad of Dermatol Venereol 2012;26:3-11.
4. Davidovici BB, Sattar N, Prinz J, Puig L, Emery P, Barker JN, *et al.* Psoriasis and systemic inflammatory diseases: potential mechanistic links between skin disease and co-morbid conditions. J Invest Dermatol 2010;130:1785-96.
5. Gelfand JM, Neimann AL, Shin DB, Wang X, Margolis DJ, Troxel AB. Risk of myocardial infarction in patients with psoriasis. JAMA 2006;296:1735-41.
6. Lindegård B. Diseases associated with psoriasis in a general population of 159,200 middle-aged, urban, native Swedes. Dermatologica 1986;172:298-304.
7. Pietrzak A, Toruniowa B, Pietrzak B, Chwaluk J. Lipid profile in psoriatic patients according to sex and age. Przegl Dermatol 1994;81:441-9.
8. Akhyani M, Ehsani AH, Robati RM, Robati AM. The lipid profile in psoriasis: a controlled study. J Eur Acad Dermatol Venereol 2007;21:1330-2.
9. Wolf N, Quaranta M, Prescott NJ, Allen M, Smith R, Burden AD, *et al.* Psoriasis is associated with pleiotropic susceptibility loci identified in type II diabetes and Crohn disease. J Med Genet 2008;45:114-6.
10. Kurd SK, Troxel AB, Crits-Christoph P, Gelfand JM. The risk of depression, anxiety, and suicidality in patients with psoriasis: a population-based cohort study. Arch Dermatol 2010;146:891-5.
11. Arias-Santiago S, Orgaz-Molina J, Castellote-Caballero L, Arrabal-Polo MÁ, García-Rodriguez S, Perandrés-López R, *et al.* Atheroma plaque, metabolic syndrome and inflammation in patients with psoriasis. Eur J Dermatol 2012;22:337-44.
12. Zdrojewski T, Rutkowski M, Bandosz P, Gaciong Z, Jędrzejczyk T, Solnica B, *et al.* Prevalence and control of cardiovascular risk factors in Poland. Assumptions and objectives of the NATPOL 2011 Survey. Kardiol Pol 2013;71:381-92.
13. Shiba M, Kato T, Funasako M, Nakane E, Miyamoto S, Izumi T, *et al.* Association between Psoriasis Vulgaris and Coronary Heart Disease in a Hospital-Based Population in Japan. PLoS One 2016;24;11: e0149316.
14. Neimann AL, Shin DB, Wang X, Margolis DJ, Troxel AB, Gelfand JM. Prevalence of cardiovascular risk factors in patients with psoriasis. J Am Acad Dermatol 2006;55:829-35.
15. Fleming P, Kraft J, Gulliver WP, Lynde C. The Relationship of Obesity With the Severity of Psoriasis: A Systematic Review. J Cutan Med Surg 2015;19:450-6.
16. Szponar-Bojda A, Krasowska D, Pietrzak A, Chodorowska G. Metabolic syndrome in psoriasis. Post Dermatol Alergol 2012;29:356-62.
17. Huskic J, Alendar F. Tissue angiotensin-converting enzyme in patients with various clinical forms of psoriasis. Bosn J Basic Med Sci 2007;7:103-6.
18. Ghafoor R, Rashid A, Anwar MI. Dyslipidemia and Psoriasis: A Case Control Study. J Coll Physicians Surg Pak 2015;25:324-7.
19. Owczarczyk-Saczonek A, Nowicki R. Prevalence of cardiovascular disease risk factors, and metabolic syndrome and its components in patients with psoriasis aged 30 to 49 years. Postep Dermatol Alergol 2015;32:290-5.
20. Janusz I, Lewandowski K, Lukamowicz J, Swiatkowska E, Narbutt J, Zalewska-Janowska A. Insulin resistance and adiponectin levels in psoriasis patients. Post Dermatol Alergol 2010;27:451-5.
21. Atas H, Kepez A, Bozbay M, Gencosmanoglu DS, Cincin A, Sunbul M, *et al.* Assessment of left atrial volume psoriasis by using real time three and function in patients with -dimensional echocardiography. Wien Klin Wochenschr 2015;127:858-63.
22. Biyik I, Narin A, Bozok MA, Ergene O. Echocardiographic and clinical abnormalities in patients with psoriasis. J Int Med Res 2006;34:632-9.
23. Shang Q, Tam LS, Sanderson JE, Lee AP, Li EK, Yu CM. Impaired left ventricular apical rotation is associated with disease activity of psoriatic arthritis. J Rheumatol 2014;41:706-13.
24. Shahidi-Dadras M, Haghighatkhah HR, Abdollahimajd F, Partovi Kia M, Zargari O. Correlation between vascular endothelial growth factor and subclinical atherosclerosis in patients with psoriasis. Int J Dermatol 2016;55:52-9.
25. Robati RM, Partovi-Kia M, Haghighatkhah HR, Younespour S, Abdollahimajd F. Increased serum leptin and resistin levels and increased carotid intima-media wall thickness in patients with pso-

riasis: is psoriasis associated with atherosclerosis? J Am Acad Dermatol 2014;71:642-8.

26. Dowlatshahi EA, Kavousi M, Nijsten T, Ikram MA, Hofman A, Franco OH, *et al.* Psoriasis is not associated with atherosclerosis and incident cardiovascular events: the Rotterdam Study. J Invest Dermatol 2013;133:2347-54.
27. Balci DD, Balci A, Karazincir S, Ucar E, Iyigun U, Yalcin F, *et al.* Increased carotid artery intima-media thickness and impaired endothelial function in psoriasis. J Eur Acad Dermatol Venereol 2009;23:1-6.
28. Troitzsch P, Paulista Markus MR, Dörr M, Felix SB, Jünger M, Schminke U, *et al.* Psoriasis is associated with increased intima- media thickness - the study of health in Pomerania (SHIP). Atherosclerosis 2012;225:486-90.
29. Enany B, El Zohiery AK, Elhilaly R, Badr T. Carotid intima-media thickness and serum leptin in psoriasis. Herz 2012;37:527-33.
30. Prodanowich S, Fangchao M, Taylor JR, Pezon C, Fasihi T, Kirsner RS. Methotrexate reduces incidence of vascular diseases in veterans with psoriasis or rheumatoid arthritis. J Am Acad Dermatol 2005;52:262-7.